SOME OF THE CHEMICAL CONSTITUENTS OF GUARANA

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The guarana used for this investigation was kindly given to me by Dr. Wolferstan Thomas, who informed me that the drug is used as a remedy against diarrhoea in Brazil. The work was carried out by me while still on the staff of the Liverpool School of Tropical Medicine, in the Runcorn Research Laboratories.

As far as my present results go, the chief and probably the effective constituent of the particular guarana[1] examined by me is the alkaloid $C_{40}H_{47}O_{21}N_4$, for which the name *β-guarinine* is suggested. The *β-guarinine* differs from Martius's[2] guarinine, isolated by him from *Paullinia sorbilis*, in that I was unable to identify it either with theine or with theobromine, whereas guarinine is, according to Berthemot and Dechatelas,[3] simply theine This is of interest, as the alkaloids both of *Paullinia sorbilis* (v. *cupana*) and *P. cambess* are either theine, theobromine, or a mixture of both alkaloids. However, it ought to be mentioned that neither of those two species of *Paullinia* are used for diarrhoea, according to Dekker,[4] who states, *only* with reference to *Paullinia trigonia*, Vellos: 'de zwak gerooste zaden teger diarrhoe.' This probably accounts for the fact that I was unable to find in the guarana I examined, an alkaloid of a known purine type.

β-guarinine

The finely powdered material was extracted with alcohol containing 1 per cent. of hydrochloric acid, at a temperature of

55 to 60° C. on the water-bath. After cooling, the calculated amount of ammonia was added and the product—a greyish powder—collected and re-dissolved in boiling alcohol. The alcoholic solution was then boiled with animal charcoal for ten to fifteen minutes, filtered and evaporated to about one-third of its volume, when on standing small needles crystallised out. These needles melted at 217° to 219°, but at a temperature of 167° to 169° a slight decomposition was noticed. The product was dried for two hours at 116°, when a loss of water of crystallisation corresponding to $2\frac{1}{2}$ molecules was observed.

The following analyses were carried out:—

I. 0·2151 gr. gave 0·3744 gr. CO_2 and 0·1065 gr. H_2O.
II. 0·2001 gr. gave 0·3474 gr. CO_2 and 0·0979 gr. H_2O.
III. 0·2337 gr. gave 0·4057 gr. CO_2 and 0·1109 gr. H_2O.
IV. 0·2211 gr. gave 18·8 c.c. N_2 (moist) at 27° C. and 741 mm.
V. 0·2473 gr. gave 20·6 c.c. N_2 (moist) at 27° C. and 741 mm.

Found C = 47·47%, 47·35%, 47·35%.
H = 5·50%, 5·44%, 5·27%.
N = 9·24%, 9·00%.

$C_{40}H_{47}O_{21}N_4$ (β-Guarinine) requires: C = 47·00%, H = 4·90%, N = 9·14%.
$C_8H_{10}O_2N_4$ (Theine) requires: C = 49·48%, H = 5·16%, N = 28·86%.
$C_7H_8O_2N_4$ (Theobromine) requires: C = 46·66%, H = 4·44%, N = 31·11%.

On boiling with acetic anhydride, β-guarinine forms an acetyl derivative—probably the monoacetyl (?)—which crystallises from alcohol in small needles and melts at 192° to 196°.

When treated with methyl iodide, β-guarinine forms the corresponding $C_{40}H_{47}O_{21}N_4CH_3I$, which is easily transformed into the free base $C_{40}H_{47}O_{21}N_4CH_3OH$ on treatment with freshly prepared Ag_2O. The base crystallises from chloroform in long needles, which melt at 167° to 168°.

Like other alkaloids, β-guarinine forms, when brominated in chloroform, a bromine derivative, probably $C_{40}H_{46}Br\ O_{21}N_4$, which crystallises from acetic acid and alcohol, and melts at 236° to 237°.

From the above analytical data it is obvious, especially from the nitrogen-figures, that β-guarinine is neither theine nor theobromine.

Similar conclusions must be drawn from a comparison of the different melting-points of β-guarinine and its derivatives, with those of theine or theobromine and their derivatives, as can be seen from the following table:—

	β-Guarinine	Theine	Theobromine
Free base	217–219°	234–235°	329–330°
Acetyl derivative	192–196°	Not known	Not known
Methyl	167–168°	137–138°	119–121°
Bromine	236–237°	206–209°	Not known

A great deal of attention has been paid by other workers to the tannic acid,[5] the so-called *guarana-tannic* acid, found in guarana, but I have been unable to confirm their results, viz., that guarana-tannic acid is identical with catechin. On the other hand, my results point more or less to the fact that this particular acid is identical with *Chlorogenic acid*, isolated by Gorter[6] from Liberian coffee-beans. Gorter has recently proved that coffee-tannic acid does not exist, and has shown this acid to be a mixture of chlorogenic and coffalic acids. He[7] has also shown the so-called *Heliant-tannic acid* from *Helianthus annuus* to be chlorogenic acid.

A quantitative estimation of the tannic acid in the guarana carried out by Körner's and Nierenstein's[8] caseine method gave 4·3 per cent., an amount which seemed to be sufficient for an attempt at isolating it. The acid was accordingly isolated by the acetone-method[9] and purified by formation of its lead salt. It represented an amorphous powder of no definite melting point. It was further purified by dissolving the product in ethyl acetate; the solution, after filtering, was evaporated to dryness and re-dissolved in boiling water, from which solution it slowly separated out in small colourless needles, which melted at 199° to 201°.

For the analysis the product was dried for two hours at 110°.

0·1886 gr. gave 0·3664 gr. CO_2 and 0·0877 gr. H_2O.

Found, C = 52·98%, H = 5·17.

$C_{32}H_{38}O_{19}$ (Chlorogenic acid) requires: C = 52·90%, H = 5·22%.

$C_{15}H_{14}O_6$ (Catechin) requires: C = 62·06%, H = 4·83%.

These results, which indicate that guarana-tannic acid may be identical with chlorogenic acid, were *not* confirmed either by formation of the acetyl derivative or the aniline salt; both preparations had quite different melting points from those given by Gorter. This leads us to the view that the tannic acid from guarana is not identical with chlorogenic acid, but that it is as an independent guarana-tannic acid; and in no case can this acid be considered to be catechin, as can be seen from the following table of melting points:—

		Acetyl derivative	Aniline salt
Guarana tannic acid	M.P. 199–201°	M.P. 147–149°	M.P. 203–205°
Chlorogenic acid	M.P. 206–207°	M.P. 180–181°	M.P. 174°
Catechin	M.P. 175–177°	M.P. 124–125°	Not known
Perkin's & Yoshitaka's higher-melting Catechin	M.P. 235–237°	Not known	Not known
Acacia Catechin	M.P. 204–205°	M.P. 158–160°	Not known

Further investigations of both the β-guarinine and the guarana-tannic acid are wanted, before a definite opinion with regard to the constitution of these two compounds can be formed; *however, in no case can the opinion be maintained that the chief constituents of this plant are theine and catechin.*

LITERATURE

1. For a full account of Guarana see P. H. Marsden. Annals of Tropical Medicine and Parasitology, Vol. IV, No. 1, p. 105.
2. Martius. Annalen der Chemie, Vol. XXXVI, p. 93.
3. Berthemiot u. Dechatelas. Jour. d. Pharm., Vol. XXVI. p. 514.
4. Dekker, I.; De Looistoffen, Vol. I, p. 149; see also Peckolt, Ber. d. deutsch. pharm. Ges., 1903, p. 339.
5. Marsden, P. H.; *loc. cit.*, and Dekker, I.; De Looistoffen, Vol. II. p. 133.
6. Gorter, K.; Annalen der Chemie, Vol. 358, p. 327, and Vol. 359, p. 217.
7. Gorter, K.; Archiv der Pharmacie, Vol. 287, p. 436.
8. Nierenstein, M. und Webster, J. A.; Collegium, p. 337, 1909, Frankfurt a. M.
9. Nierenstein M.; Darstellung u. Nachweis der Gerbstoffe Abderhalden, Handbuch der biochemischen Arbeitsmethoden, Bd. II, S. 996.